Repolarization in Patients with Ischemic and Non-Ischemic Cardiomyopathy

Niederseer, David ; Rossi, Valentina A ; Barbier, F ; Schmied, Christian M ; Bohm, Philipp ; et al

DOI: https://doi.org/10.4414/cvm.2020.02129

Cardiovascular Medicine

Original article | Published 10 September 2020 | doi:10.4414.cvm.2020.02129
Cite this as: Cardiovasc Med. 2020;23:w02129

Repolarisation in patients with ischaemic and nonischaemic cardiomyopathy: assessment of parameters of transmural dispersion of repolarisation using the 65-lead surface ECG

Niederseer David[a], Rossi Valentina A.[a], Barbieri Fabian[b], Schmied Christian M.[a], Bohm Philipp[a], Pfeifer Bernhard[cd], Wernly Bernhard[e], Dichtl Wolfgang[b], Stuhlinger Markus[b], Hintringer Florian[b], Berger Thomas[fg]

[a] Department of Cardiology, University Heart Centre, Zurich, Switzerland
[b] Department of Internal Medicine III, Cardiology and Angiology, Medical University Innsbruck, Austria
[c] Institute of Electrical and Biomedical Engineering, UMIT, Hall in Tyrol, Austria
[d] Institute for Integrated Care, Tirol Kliniken, Austria
[e] Department of Internal Medicine II, Paracelsus Medical University Salzburg, Austria
[f] Medical Department, Hospital Barmherzige Brueder, Linz, Austria
[g] Department of Rehabilitation, Cardiomed Rehabilitation Centre, Linz, Austria

Summary

BACKGROUND: Patients with heart failure and reduced ejection fraction (HFrEF) are at-risk for arrhythmic events. The aetiology corresponds to incidence of sudden cardiac death and effectiveness of shock therapy. We aimed to investigate repolarisation patterns in HFrEF patients with ischaemic (ICMP) or nonischaemic dilated cardiomyopathy (DCMP) using high-resolution 65-lead surface electrocardiography.

METHODS: Fifty-six patients with heart failure underwent coronary angiography and were treated with optimised heart failure medication. Forty-two patients (13 female, mean age 65.1 ± 10.7 years, left ventricular ejection fraction 22.5 ± 6.5%) were then further stratified according to QRS duration (n = narrow QRS complex <120 ms; w = wide QRS complex >120 ms). Patients were divided into four groups: wICMP, n = 12; nICMP, n = 10; wDCMP: n = 10; nDCMP: n = 10. Using a high-resolution electrocardiogram we estimated measures of parameters of transmural dispersion of repolarisation.

RESULTS: At baseline, groups were comparable except for variables related to group distribution. No difference in heart rate or T wave duration could be detected. However, the Tpeak-Tend interval differed significantly between groups (nICMP vs wICMP: p = 0.030; nDCMP vs wDCMP: p <0.001), and also in nICMP vs nDCMP (p = 0.021). If DCMP and ICMP were grouped regardless of QRS width, the Tpeak-Tend interval also differed significantly (p = 0.035). Follow-up of 10 years revealed no difference between Tpeak-Tend interval, QRS-duration or aetiology of heart failure in a combined endpoint of death, ventricular arrhythmia or implantable cardioverter defibrillator therapy. However, there was a significant difference for death between ICMP (n = 4, 19% vs DCMP (n = 0, 0%; p = 0.045).

CONCLUSION: ICMP had a longer Tpeak-Tend duration and Tpeak-Ten -integral compared with DCMP despite normal parameters of depolarisation (QRS duration/integral). This may reflect different arrhythmogenic morphological substrates and explain why ventricular tachycardias are more common in ICMP.

Keywords: *ischaemic cardiomyopathy*, *dilated cardiomyopathy*, *dispersion of repolarisation*, *sudden cardiac death*

Correspondence:
Correspondence:, *Universitäres Herzzentrum* , *UniversitätsSpital*, *CH-8091 Zurich*, *david.niederseer[at]usz.ch*

Introduction

Cardiovascular diseases are responsible for more than 30% of deaths worldwide and among these about 25% are sudden cardiac deaths (SCDs) [1, 2]. Coronary artery disease accounts for a large proportion of SCDs, especially in patients older than 40 years, mainly because of the acute development of malignant arrhythmias during or immediately after physical exercise, probably due to ischaemic triggers [3]. However, 10% of cases of SCD are associated with cardiomyopathies of other aetiologies. It has been postulated that arrhythmias possibly arise from the synergetic activation of the sympathetic nervous and renin-angiotensin systems acting on a sensitised underlying mechanical substrate and leading to disorganised electrical activity, resulting in malignant arrhythmias and SCD. In both ischaemic and nonischaemic cardiomyopathies, fibrosis and myocardial scars have been identified as a substrate for adverse arrhythmic events. In contrast to scar-related macro-reentrant ventricular tachycardia in ischaemic cardiomyopathy, the mechanisms of arrhythmias in patients with nonischaemic cardiomyopathy are as yet not well understood [4].

ECG repolarisation indices have repeatedly been the focus for prediction of malignant ventricular arrhythmias and SCD [5]. There is preliminary evidence that a prolongation of transmural dispersion of repolarisation is independently linked with an increased risk of ventricular arrhythmia and SCD in patients with either ischaemic or nonischaemic cardiomyopathies, as well as in the general population [6, 7] However, most ECG-derived analysis of parameters of the transmural dispersion of ventricular repolarisation have been carried out using the standard 12-lead surface ECG with a focus at the anterior wall (lead V5) [8]. Therefore, more comprehensive changes of repolarisation may have been previously missed. To address this uncertainty, we compared parameters of transmural dispersion of repolarisation in patients with ischaemic and nonischaemic cardiomyopathy by using a high-resolution 65-lead surface ECG.

Methods

Study population

Patients previously diagnosed with cardiomyopathy due to coronary artery disease (ICMP) or with cardiomyopathy of nonischaemic origin (DCMP) and who underwent a regular follow-up in our outpatient clinic were included in this study in 2001. These patients were eligible if they were aged between 18 and 80 years, and had a left ventricular ejection fraction (LVEF) of <35%, measured either invasively (laevocardiography) or noninvasively (e.g., echocardiography, magnetic resonance imaging). Patients who were pacemaker-dependent, presented with bundle branch block and/or suffered from atrial fibrillation were excluded. The study was conducted according to the Declaration of Helsinki and was approved by the local research ethics committee. Written informed consent was obtained from all participants. For follow-up, we consulted the digital patient charts in June 2019. Here we assessed the last follow-up visit where the patient was alive, the date and cause of death and if the patients had cardiac arrhythmias or implantable cardioverter defibrillator (ICD) therapies. Relevant cardiac arrhythmias were defined as definitive ventricular arrhythmia and sub-grouped into sustained (>30 seconds) or nonsustained (<30 seconds) ventricular tachycardia. ICD therapies were assessed by reviewing ICD interrogation documents and ICD therapy was defined as antitachycardia pacing and/or adequate shock.

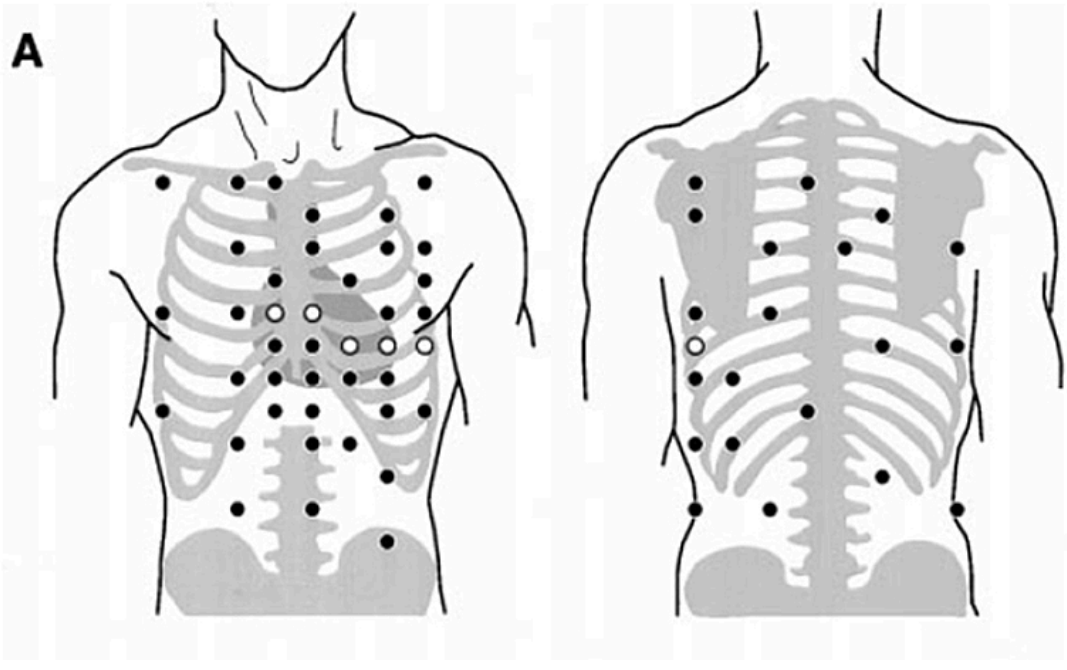
Study design

Electrocardiographic data recording

In order to eliminate any electromagnetic interference in the investigation room, all electrical devices were switched off. The room was silent. The room temperature was set at the same level for all measurements and the lights were turned off. All measurements were performed between 13:00 and 16:00. Patients were asked to abstain from tobacco, caffeine or alcohol intake on the day of the study.

A high-resolution 65-lead body-surface ECG was recorded for each patient with a computer-based recording and analysis system (Biosemi V.O.F., The Netherlands) [9, 10]. In total, 14 vertical self-adhesive straps with 65 unipolar electrodes were placed on the patient's torso as shown in figure 1, starting from the vertebral column with the patient in the sitting position. The other electrodes were added with the patient lying down in a recumbent position. Four electrodes were placed on the extremities according to Einthoven. The electrodes D5, E5, F6, G6, H6 and I6

Figure 1: A high-resolution 65-lead body-surface ECG was recorded for each patient with a computer-based recording and analysis system (Biosemi V.O.F., The Netherlands). Fourteen vertical self-adhesive straps with 65 electrodes were placed on the patient's torso, as shown in this figure, starting from the vertebral column with the patient in the sitting position. The other electrodes were added with the patient lying down in a recumbent position. Four electrodes were placed on the extremities according to Einthoven. The electrodes D5, E5, F6, G6, H6 and I6 were placed according to Wilson's leads (where electrode "D5" was equivalent to Wilson's "V1").



were placed according to Wilson's leads (where electrode "D5" was equivalent to Wilson's "V1"), as previously described [10].

After patients had been lying for 5 minutes in a relaxed supine position, recordings were started and continued for at least 30 seconds. In patients with a cardiac device, the device was switched off after all the leads had been attached. After 90 seconds the signal was measured. Lead placement was optimised until all leads produced an acceptable signal. If we were unable to reduce the noise in all leads, we accepted a maximum number of 5–7 leads with noise (i.e., 10%). We used 10 seconds of recording and analysed three heart cycles. All measurements were performed by one observer.

Measurements of systolic left ventricular function

Echocardiographic measurements were made by experienced cardiologists and were performed within 3 months from study beginning. LVEF was determined with the biplane Simpson's method. In every patient, coronary angiography had previously been performed in order to diagnose or rule out underlying coronary artery disease.

Data analysis

Details on the analysis, processing and calculation of the 65-lead ECG data are provided elsewhere [10]. As the presence of bundle branch block (and consequently a narrow or wide QRS complex) obviously influences repolarisation patterns, we grouped our subjects according to the width of the QRS complex: wide (>120ms) or narrow (<120ms). Thereafter we compared patients with ischaemic and nonischaemic cardiomyopathy, resulting in four groups. The following parameters were assessed in all four groups: QRS duration, QRS integral, RR interval, QT_c duration, JT duration, JT integral, Tpeak-Tend duration, Tpeak-Tend integral.

QRS duration was determined from the beginning of the QRS complex to the J point. The onset of QRS, J point and offset of the T wave were identified manually from the root mean square (RMS) signal. The QT_c was calculated using Bazett's formula. The peak of the T wave was computed as the maximum RMS signal voltage of the ST-T interval where the RMS signal had the maximum value. RMS and the area under QRS complex, JT integral and Tpeak-Tend interval (integral) were calculated. Multiple measurements of the parameters were made and mean values were used for statistical analysis. If the onset or offset of a parameter was not clear in the RMS graph, callipers were adjusted according to the adjacent leads on the torso.

All data were analysed and processed off-line by the signal-processing tool ViewEDF, developed by UMIT (University for Health Informatics and Technology Tyrol, Institute for Medical Signal Processing and Imaging; Hall, Austria).

The RMS was calculated according to the formula below (figure 2) from all 65 leads using Matlab software 6.0 (The MathWorks, Inc., Natick, MA); leads with poor signal quality were excluded.

Statistical analysis

Statistical analysis was performed with GraphPad InStat version 3.06 for Windows, San Diego, California, USA and SPSS, 2010, SPSS 18.0.2 for Windows, SPSS Inc., Armonk, NY, USA. Data are presented as mean (± standard deviation [SD]) and percentages, as appropriate. Correlations between quantitative variables were calculated by standard linear regression analysis. Differences in baseline characteristics and comparisons of changes between groups were assessed by paired or independent t-tests, as appropriate. Categorical data were compared using the chi-square test. A two-sided p-value of <0.05 was considered to be statistically significant.

Figure 2: RMS calculation. N = number of analysed channels, v_i = voltage [mV] of lead i.

$$RMS(t) = \sqrt{\frac{\sum_{i=1}^{n} v_i^2(t)}{N}}$$

Results

Population

Forty-two patients were included and categorised into four groups depending on the aetiology of cardiomyopathy and QRS complex width (measured on 12-lead surface ECG). The groups were defined as follows: patients with ischaemic cardiomyopathy and a narrow QRS <120 ms (nICMP); patients with ischaemic cardiomyopathy and a wide QRS >120 ms (wICMP,); patients with nonischaemic cardiomyopathy and a narrow QRS <120 ms (nDCMP); and patients with nonischaemic cardiomyopathy and a wide QRS >120 ms (wDCMP). Examples of 12-lead surface ECGs from each of the four groups are shown in figure 3. Baseline characteristics are summarised in table 1. In total, 56 patients were screened, 14 patients were excluded because of pacemaker dependency, atrial fibrillation and/or transient bundle branch block. Subjects with cardiac resynchronisation therapy or a pacemaker were investigated in intrinsic sinus rhythm. Subjects where then allocated to the four prespecified groups.

In this observational study we found that, if matched for the aetiology of the underlying cardiomyopathy, patients with a wide QRS complex >120 ms had a statistically significantly longer Tpeak-Tend interval and Tpeak-Tend integral compared with those with a narrow QRS complex (wICMP vs nICMP, p = 0.03; wDCMP vs nDCMP, p <0.001). Interestingly, patients with ischaemic cardiomyopathy and a narrow QRS complex also had a statistically significantly longer Tpeak-Tend interval and Tpeak-Tend-integral than patients with a narrow QRS complex and nonischaemic cardiomyopathy (nICMP vs nDCMP, p<0.001). However, irrespective of underlying cardiomyopathy both groups with widened a QRS complex >120ms showed evidence of prolonged parameters of transmural dispersion of repolarisation (p = 0.816). Electrocardiographic characteristics are summarised in table 2.

Arrhythmogenic events were recorded after a mean follow-up of 10 years for 40 patients out of 42 (95%). Arrhythmogenic events were recorded after a mean follow-up of 10 years for 40 patients out of 42 (95%). In total, 13 patients (31%) had any documented arrhythmia of ventricular origin, therapy from an implanted defibrillator or death. In total, 11 patients experienced ventricular tachycardia (9

non-sustained ventricular tachycardia, 6 sustained ventricular tachycardia; 4 patients had both sustained and non-sustained ventricular tachycardia). Furthermore, 6 patients received a therapy from an implanted defibrillator, and 4 patients died. As outcomes overlapped (i.e. a patient had ICD-therapies prior to death), the numbers do not add up to the sum of 13.No differences for the combined endpoint of ventricular arrhythmia, ICD therapy or death were found with respect to QRS duration, Tpeak-Tend interval and aetiology of cardiomyopathy. However, a statistically significant difference for death in patients with ischaemic cardiomyopathy as compared with those with nonischaemic cardiomyopathy was observed (p = 0.045, 4, 19% vs 0, 0%).

Figure 3: Examples of 12-lead surface ECGs of the four groups: patients with ischaemic cardiomyopathy and narrow a QRS <120 ms (nICMP); patients with ischaemic cardiomyopathy and a wide QRS >120 ms (wICMP); patients with nonischaemic cardiomyopathy and a narrow QRS <120 ms (nDCMP); and patients with nonischaemic cardiomyopathy and a wide QRS >120 ms (wDCMP).

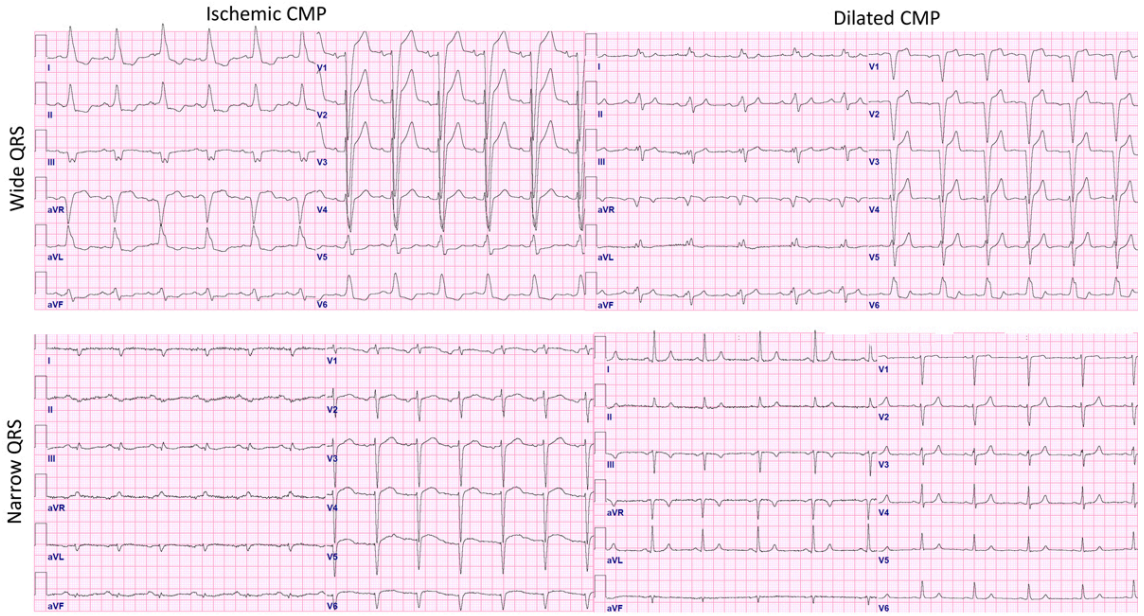


Table 1: Baseline characteristics.

	nICMP (n = 10)	wICMP (n = 12)	nDCMP (n = 10)	wDCMP (n = 10)
Age (years)	65 ± 10.5	69 ± 4.8	57 ± 12.8	68 ± 11
Male (%)	60	83	70	60
LVEF (%)	25 ± 5	22 ± 7	25 ± 6	21 ± 6
CRT/PM (n)	1/0	6/3	1/0	6/4
ICD	3	4	0	3
Beta-blockers	2/10	9/12	6/10	8/10
Diuretics	2/10	10/12	3/10	7/10
ACE inhibitors / sartans	1/10	9/12	7/10	8/10
Amiodarone	4/10	4/12	2/10	0
Spironolactone	3/10	3/12	0	5/10

ACE = angiotensin converting-enzyme; CRT/PM = cardiac resynchronisation therapy/pacemaker; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction. Values are mean ± standard deviation or percent as appropriate; p >0.05 for all comparisons.

Table 2: ECG characteristics.

	nICMP (n = 10)	wICMP (n = 12)	nDCMP (n = 10)	wDCMP (n = 10)	nICMP vs wICMP	nICMP vs nDCMP	nICMP vs wDCMP	wICMP vs wDCMP	nDCMP vs wDCMP
QRS duration (ms)	104 ± 11	163 ± 24	103 ± 12	170 ± 20	p <0.05	n.s.	p <0.05	p <0.05	p <0.05
QRS integral	30 ± 14	79 ± 31	34 ± 13	87 ± 22	P <0.05	n.s.	p <0.05	p <0.05	p <0.05
JT duration (ms)	301 ± 34	303 ± 52	295 ± 55	269 ± 30	n.s.	n.s.	p <0.05	p <0.05	p <0.05
T duration (ms)	302 ± 29	303 ± 52	295 ± 55	269 ± 30	n.s.	n.s.	p <0.05	n.s.	n.s.
T integral	30 ± 9	73 ± 29	30 ± 15	76 ± 28	p <0.05	n.s.	p <0.05	p <0.05	p <0.05
Tp-Te interval (ms)	109 ± 10	124 ± 19	76 ± 7&	126 ± 20	p <0.05	p <0.05	p <0.05	p <0.05	p <0.05
Tp-Te integral	10 ± 4	24 ± 11	7 ± 3	30 ± 16	p <0.05	n.s.	p <0.05	p <0.05	p <0.05
QT_c duration (ms)	438 ± 50	488 ± 45	412 ± 40	470 ± 47	p <0.05	n.s.	n.s.	p <0.05	p <0.05
Heart rate /min	73 ± 19	68 ± 16	70 ± 29	70 ± 12	n.s.	n.s.	n.s.	n.s.	n.s.

nICMP = ischaemic cardiomyopathy with normal QRS complex; wICMP = ischaemic cardiomyopathy with widened QRS complex; nDCMP = dilated cardiomyopathy with normal QRS complex; wDCMP = dilated cardiomyopathy with widened QRS complex; Tp-Te = Tpeak to Tend Values are mean ± standard deviation.

Discussion

It is of prognostic and therapeutic relevance to be able to distinguish between ischaemic and nonischaemic cardiomyopathy, particularly as SCD is one of the leading causes of death in patients with ischaemic cardiomyopathy. To date, several noninvasive markers have been considered for risk stratification. Recent data from the DANISH trial suggested that ischemic cardiomyopathy patients might in general benefit from wider use of ICD therapy, whereas only subgroups of nonischaemic cardiomyopathy patients showed beneficial effects [11].

There is growing evidence that an increase in dispersion of ventricular repolarisation, as reflected by the Tpeak-Tend interval, represents a more reliable independent predictor for malignant arrhythmias compared to QT_c time in patients with Brugada syndrome, hypertrophic cardiomyopathy, heart failure with preserved ejection fraction (HFpEF), long QT syndrome and ischaemic cardiomyopathy [12–17]. In "*in vitro* experiments", Tpeak-Tend has been established to be a measure of transmural dispersion of repolarisation due to a gradient in action potential duration from endocardial cells to epicardial and to midmyocardial M-cells [18, 19] [20]. Lately, the Tpeak-Tend interval has rather been suggested as an index of overall global heterogeneity of ventricular repolarisation across the three dimensions of the intact heart *in vivo* [21, 22].

However, amplification of the dispersion of ventricular repolarisation has long been known as a favourable electrophysiological substrate for the onset of malignant re-entry arrhythmias. The combination of unfavourable mechanical and electrical remodelling has been hypothesised on the basis of findings in isolated wedge preparations of failing human hearts, and impaired contractility has been related to alterations of transmural dispersion of repolarisation and impaired calcium handling across the different transmural layers. This effect has also been demonstrated in a randomised controlled trial, in which alteration in the dispersion of repolarisation has been positively associated with mechanical wall stress during obstructive apnoea [23, 24].

In our study we postulated the existence of different mechanical substrates due to either ischaemic or nonischaemic heart disease. We demonstrated an association of repolarisation abnormalities by analysing different parameters of transmural dispersion of repolarisation using a 65-lead ECG, which allowed more reliable calculations by limiting systematic errors due to unclear T wave offset [9]. We found that patients with coronary artery disease had a significantly prolonged Tpeak-Tend duration and Tpeak-Tend integral compared with patients with cardiomyopathy from other causes, despite normal parameters of depolarisation.

In a prospective study including 1570 patients with heart failure due to both dilated and ischaemic cardiomyopathy (mean LVEF 32% and 44%, respectively), Tpeak-Tend duration was found to be significantly longer in those who experienced SCD or appropriate cardioverter defibrillator discharge compared with healthy controls. However, this trial failed to find a prognostic value of prolongation in dispersion of repolarisation, possibly owing to a relatively preserved ejection fraction, indicating a not yet deranged mechanical ventricular remodelling [25]. In contrast, in another clinical study with a similar population but with a mean LVEF of 23%, a longer Tpeak-Tend interval measured during spontaneous rhythm predicted the onset of malignant arrhythmia as well as an increased overall mortality, even after correction for other independent predictors [26]. Recently, in a large prospective study including more than 138,000 individuals older than 50 years presenting to primary care, a U-shaped association between Tpeak-Tend duration and the risk of all-cause mortality, cardiovascular death and heart failure was found [27]. These findings have been confirmed in a recent meta-analysis analysing risk of SCD from 33 prospective and retrospective studies. A prolonged Tpeak-Tend interval was found to be associated with a 1.14-fold higher risk of SCD or malignant ventricular arrhythmia independently of characteristics of the populations [28].

In our small study, we found a statistically significant increase in parameters of dispersion of repolarisation in patients with heart failure due to ischaemic heart disease, regardless of alterations in depolarisation as defined by QRS width. This finding may reflect a specific arrhythmogenic morphological substrate attributable to ischaemic cardiomyopathy. Several animal studies have tried to address this hypothesis. In a porcine model of myocardial infarction, acute ischaemia resulted in an increase in dispersion of repolarisation and was postulated to contribute to ventricular fibrillation, possibly by facilitating the onset of a unidirectional conduction block [29]. In another animal model, Tpeak-Tend duration strongly correlated with the invasively measured increase in ventricular dispersion of repolarisation caused by bilateral sympathetic nerve stimulation [30]. Therefore, this may directly reflect increased sympathetic nerve activation, a common condition after myocardial infarction, possibly leading to SCD [31]. Further studies suggested that measurement of Tpeak-Tend interval seems to be an appropriate tool for arrhythmogenic risk stratification in patients who suffered acute myocardial ischaemia even after successful reperfusion treatment. This increased risk may also be increased due to a post-ischaemic disadaptive chronic activation of the sympathetic nervous system [32–34]. This could be one reason why patients with heart failure due to ischaemic cardiomyopathy are at higher risk for ventricular arrhythmias than a matched population with heart failure due to other causes, despite having no signs of ventricular remodelling (like, for example, bundle branch block).

Not surprisingly, we found that a QRS duration >120ms was related to an increase in parameters of dispersion of repolarisation independently of the aetiology of heart failure. Cardiac dyssynchrony is a known unfavourable prognostic factor in heart failure and resynchronisation therapy is, by now, a well-established therapy with a high level of recommendation for these patients [35]. There is also evidence regarding a beneficial effect of resynchronisation therapy on dispersion of ventricular repolarisation [36]. In ischaemic and nonischaemic patients, QRS widening due to QRS fragmentation indicated a worse prognosis and may reflect electromechanical remodelling due to myocardial scarring [25, 37].

We found a significant increase in mortality in patients with ischaemic cardiomyopathy as compared with patients with dilated cardiomyopathy. In line with the DANISH

trial, which showed that in dilated cardiomyopathy ICDs were not associated with a significantly lower long-term rate of death from any cause than was usual clinical care [38], our results also indicate that the ischaemic cause of heart failure is especially vulnerable to arrhythmic events. No differences were found, however, based on QRS duration. This might be explained by the small size of our population.

The Tpeak-Tend interval helps to identify these detrimental myocardial and electrical remodelling effects independently of the underlying aetiology. Therefore, measurement of Tpeak-Tend interval may help to further improve risk stratification on an individual basis.

Some confounding factors must be considered. Firstly, this was a small observational study with limited data, and unknown confounders related to a small sample size might have influenced the results. Furthermore, we did not have data on myocardial scaring (cardiac magnetic resonance imaging or voltage maps from invasive electrophysiological studies).The percentage of atrial, right and left ventricular pacing before the 65-lead ECG had not been recorded. Also, several methodological limitations also apply. We used a standardised protocol for the application of the vertical electrode strips; however, slight variability due to body size and shape are possible. Confounding of T wave memory might apply to our patients with cardiac devices. Because of time restraints and also the safety of the patients, we refrained from waiting longer with a deactivated device. We therefore cannot rule out some T wave memory effects that might have confounded our results.

However, the strength of the study was the very long follow up. The identification of the T wave offset was sometimes problematic, which may have resulted in intraobserver and interobserver variability. To adjust for this limitation multiple measurements were performed and average values were used for statistical analysis.

Finally, there is a circadian variability in both depolarisation and repolarisation characteristics. Measurements in our study were performed in the early afternoon on a routinely basis.

Conclusion

In this study we analysed different parameters of the transmural dispersion of repolarisation by using a high-resolution 65-lead ECG, which allowed more reliable calculations by reducing systematic errors due to unclear T wave offset. We found that patients with ischaemic heart failure show statistically significant prolonged Tpeak-Tend duration and Tpeak-Tend integral values as compared with nonischaemic heart failure patients, despite normal parameters of depolarisation. This may reflect the different arrhythmogenic morphological substrate, and explain why ventricular tachycardia is much more common in ischaemic cardiomyopathy. These data may provide further evidence for the detection and stratification of patients who could benefit from prophylactic implantation of defibrillator.

Disclosure statement
No financial support and no conflict of interest relevant to this article was reported.

References

1 McMurray JJ, Petrie MC, Murdoch DR, Davie AP. Clinical epidemiology of heart failure: public and private health burden. Eur Heart J. 1998;19(Suppl P):9–16. PubMed.
2 Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. J Am Coll Cardiol. 1993;22(4, Suppl A):A6–A13. doi: http://dx.doi.org/10.1016/0735-1097(93)90455-A. PubMed.
3 Gorenek B, Blomström Lundqvist C, Brugada Terradellas J, Camm AJ, Hindricks G, Huber K, et al. Cardiac arrhythmias in acute coronary syndromes: position paper from the joint EHRA, ACCA, and EAPCI task force. Europace. 2014;16(11):1655–73. doi: http://dx.doi.org/10.1093/europace/euu208. PubMed.
4 Halliday BP, Cleland JGF, Goldberger JJ, Prasad SK. Personalizing Risk Stratification for Sudden Death in Dilated Cardiomyopathy: The Past, Present, and Future. Circulation. 2017;136(2):215–31. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.116.027134. PubMed.
5 Wu SH, Lin XX, Cheng YJ, Qiang CC, Zhang J. Early repolarization pattern and risk for arrhythmia death: a meta-analysis. J Am Coll Cardiol. 2013;61(6):645–50. doi: http://dx.doi.org/10.1016/j.jacc.2012.11.023. PubMed.
6 Mikuz U, Poglajen G, Fister M, Starc V, Wu JC, Hsia H, et al. The presence of electromechanical mismatch in nonischemic dilated cardiomyopathy is associated with ventricular repolarization instability. J Card Fail. 2014;20(12):891–8. doi: http://dx.doi.org/10.1016/j.cardfail.2014.10.002. PubMed.
7 Porthan K, Viitasalo M, Toivonen L, Havulinna AS, Jula A, Tikkanen JT, et al. Predictive value of electrocardiographic T-wave morphology parameters and T-wave peak to T-wave end interval for sudden cardiac death in the general population. Circ Arrhythm Electrophysiol. 2013;6(4):690–6. doi: http://dx.doi.org/10.1161/CIRCEP.113.000356. PubMed.
8 Owens C, McClelland A, Walsh S, Smith B, Adgey J. Comparison of value of leads from body surface maps to 12-lead electrocardiogram for diagnosis of acute myocardial infarction. Am J Cardiol. 2008;102(3):257–65. doi: http://dx.doi.org/10.1016/j.amjcard.2008.03.046. PubMed.
9 SippensGroenewegen A, Peeters HA, Jessurun ER, Linnenbank AC, Robles de Medina EO, Lesh MD, et al. Body surface mapping during pacing at multiple sites in the human atrium: P-wave morphology of ectopic right atrial activation. Circulation. 1998;97(4):369–80. doi: http://dx.doi.org/10.1161/01.CIR.97.4.369. PubMed.
10 Berger T, Fischer G, Pfeifer B, Modre R, Hanser F, Trieb T, et al. Single-beat noninvasive imaging of cardiac electrophysiology of ventricular pre-excitation. J Am Coll Cardiol. 2006;48(10):2045–52. doi: http://dx.doi.org/10.1016/j.jacc.2006.08.019. PubMed.
11 Køber L, Thune JJ, Nielsen JC, Haarbo J, Videbæk L, Korup E, et al.; DANISH Investigators. Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure. N Engl J Med. 2016;375(13):1221–30. doi: http://dx.doi.org/10.1056/NEJMoa1608029. PubMed.
12 Castro Hevia J, Antzelevitch C, Tornés Bárzaga F, Dorantes Sánchez M, Dorticós Balea F, Zayas Molina R, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. J Am Coll Cardiol. 2006;47(9):1828–34. doi: http://dx.doi.org/10.1016/j.jacc.2005.12.049. PubMed.
13 Rosenthal TM, Stahls PF, 3rd, Abi Samra FM, Bernard ML, Khatib S, Polin GM, et al. T-peak to T-end interval for prediction of ventricular tachyarrhythmia and mortality in a primary prevention population with systolic cardiomyopathy. Heart Rhythm. 2015;12(8):1789–97. doi: http://dx.doi.org/10.1016/j.hrthm.2015.04.035. PubMed.
14 Yamaguchi M, Shimizu M, Ino H, Terai H, Uchiyama K, Oe K, et al. T wave peak-to-end interval and QT dispersion in acquired long QT syndrome: a new index for arrhythmogenicity. Clin Sci (Lond). 2003;105(6):671–6. doi: http://dx.doi.org/10.1042/CS20030010. PubMed.
15 Ferrucci A, Canichella F, Battistoni A, Palano F, Francia P, Ciavarella GM, et al. A Novel Electrocardiographic T-Wave Measurement (Tp-Te Interval) as a Predictor of Heart Abnormalities in Hypertension: A New Opportunity for First-Line Electrocardiographic Evaluation. J Clin Hypertens (Greenwich). 2015;17(6):441–9. doi: http://dx.doi.org/10.1111/jch.12522. PubMed.
16 Saba MM, Arain SA, Lavie CJ, Abi-Samra FM, Ibrahim SS, Ventura HO, et al. Relation between left ventricular geometry and transmural dispersion of repolarization. Am J Cardiol. 2005;96(7):952–5. doi: http://dx.doi.org/10.1016/j.amjcard.2005.05.053. PubMed.
17 Oskouie SK, Prenner SB, Shah SJ, Sauer AJ. Differences in Repolarization Heterogeneity Among Heart Failure With Preserved Ejection Frac-

tion Phenotypic Subgroups. Am J Cardiol. 2017;120(4):601–6. doi: http://dx.doi.org/10.1016/j.amjcard.2017.05.031. PubMed.

18 Antzelevitch C, Sicouri S, Litovsky SH, Lukas A, Krishnan SC, Di Diego JM, et al. Heterogeneity within the ventricular wall. Electrophysiology and pharmacology of epicardial, endocardial, and M cells. Circ Res. 1991;69(6):1427–49. doi: http://dx.doi.org/10.1161/01.RES.69.6.1427. PubMed.

19 Yan GX, Antzelevitch C. Cellular basis for the normal T wave and the electrocardiographic manifestations of the long-QT syndrome. Circulation. 1998;98(18):1928–36. doi: http://dx.doi.org/10.1161/01.CIR.98.18.1928. PubMed.

20 Antzelevitch C. Role of spatial dispersion of repolarization in inherited and acquired sudden cardiac death syndromes. Am J Physiol Heart Circ Physiol. 2007;293(4):H2024–38. doi: http://dx.doi.org/10.1152/ajpheart.00355.2007. PubMed.

21 Antzelevitch C, Sicouri S, Di Diego JM, Burashnikov A, Viskin S, Shimizu W, et al. Does Tpeak-Tend provide an index of transmural dispersion of repolarization? Heart Rhythm. 2007;4(8):1114–6, author reply 1116–9. doi: http://dx.doi.org/10.1016/j.hrthm.2007.05.028. PubMed.

22 Xia Y, Liang Y, Kongstad O, Holm M, Olsson B, Yuan S. Tpeak-Tend interval as an index of global dispersion of ventricular repolarization: evaluations using monophasic action potential mapping of the epi- and endocardium in swine. J Interv Card Electrophysiol. 2005;14(2):79–87. doi: http://dx.doi.org/10.1007/s10840-005-4592-4. PubMed.

23 Lou Q, Fedorov VV, Glukhov AV, Moazami N, Fast VG, Efimov IR. Transmural heterogeneity and remodeling of ventricular excitation-contraction coupling in human heart failure. Circulation. 2011;123(17):1881–90. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.110.989707. PubMed.

24 Rossi VA, Stoewhas AC, Camen G, Steffel J, Bloch KE, Stradling JR, et al. The effects of continuous positive airway pressure therapy withdrawal on cardiac repolarization: data from a randomized controlled trial. Eur Heart J. 2012;33(17):2206–12. doi: http://dx.doi.org/10.1093/eurheartj/ehs073. PubMed.

25 Pei J, Li N, Gao Y, Wang Z, Li X, Zhang Y, et al. The J wave and fragmented QRS complexes in inferior leads associated with sudden cardiac death in patients with chronic heart failure. Europace. 2012;14(8):1180–7. doi: http://dx.doi.org/10.1093/europace/eur437. PubMed.

26 Morin DP, Saad MN, Shams OF, Owen JS, Xue JQ, Abi-Samra FM, et al. Relationships between the T-peak to T-end interval, ventricular tachyarrhythmia, and death in left ventricular systolic dysfunction. Europace. 2012;14(8):1172–9. doi: http://dx.doi.org/10.1093/europace/eur426. PubMed.

27 Bachmann TN, Skov MW, Rasmussen PV, Graff C, Pietersen A, Lind B, et al. Electrocardiographic Tpeak-Tend interval and risk of cardiovascular morbidity and mortality: Results from the Copenhagen ECG study. Heart Rhythm. 2016;13(4):915–24. doi: http://dx.doi.org/10.1016/j.hrthm.2015.12.027. PubMed.

28 Tse G, Gong M, Wong WT, Georgopoulos S, Letsas KP, Vassiliou VS, et al. The T_{peak} - T_{end} interval as an electrocardiographic risk marker of arrhythmic and mortality outcomes: A systematic review and meta-analysis. Heart Rhythm. 2017;14(8):1131–7. doi: http://dx.doi.org/10.1016/j.hrthm.2017.05.031. PubMed.

29 Azarov JE, Demidova MM, Koul S, van der Pals J, Erlinge D, Platonov PG. Progressive increase of the Tpeak-Tend interval is associated with ischaemia-induced ventricular fibrillation in a porcine myocardial infarction model. Europace. 2018;20(5):880–6. doi: http://dx.doi.org/10.1093/europace/eux104. PubMed.

30 Yagishita D, Chui RW, Yamakawa K, Rajendran PS, Ajijola OA, Nakamura K, et al. Sympathetic nerve stimulation, not circulating norepinephrine, modulates T-peak to T-end interval by increasing global dispersion of repolarization. Circ Arrhythm Electrophysiol. 2015;8(1):174–85. doi: http://dx.doi.org/10.1161/CIRCEP.114.002195. PubMed.

31 Vaseghi M, Shivkumar K. The role of the autonomic nervous system in sudden cardiac death. Prog Cardiovasc Dis. 2008;50(6):404–19. doi: http://dx.doi.org/10.1016/j.pcad.2008.01.003. PubMed.

32 Erikssen G, Liestøl K, Gullestad L, Haugaa KH, Bendz B, Amlie JP. The terminal part of the QT interval (T peak to T end): a predictor of mortality after acute myocardial infarction. Ann Noninvasive Electrocardiol. 2012;17(2):85–94. doi: http://dx.doi.org/10.1111/j.1542-474X.2012.00493.x. PubMed.

33 Oikarinen L, Nieminen MS, Viitasalo M, Toivonen L, Wachtell K, Papademetriou V, et al. Relation of QT interval and QT dispersion to echocardiographic left ventricular hypertrophy and geometric pattern in hypertensive patients. The LIFE study. The Losartan Intervention For Endpoint Reduction. J Hypertens. 2001;19(10):1883–91. doi: http://dx.doi.org/10.1097/00004872-200110000-00025. PubMed.

34 Tatlisu MA, Özcan KS, Güngör B, Ekmekçi A, Çekirdekçi EI, Aruğarslan E, et al. Can the T-peak to T-end interval be a predictor of mortality in patients with ST-elevation myocardial infarction? Coron Artery Dis. 2014;25(5):399–404. doi: http://dx.doi.org/10.1097/MCA.0000000000000101. PubMed.

35 Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al.; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129–200. doi: http://dx.doi.org/10.1093/eurheartj/ehw128. PubMed.

36 Berger T, Zwick RH, Poelzl G, Hoertnagl H, Pachinger O, Stuhlinger M, et al. Impact of all-day physical activity on ventilatory perfusion coupling in patients undergoing cardiac resynchronization therapy. Cardiology. 2008;111(1):68–74. doi: http://dx.doi.org/10.1159/000113431. PubMed.

37 Das MK, Suradi H, Maskoun W, Michael MA, Shen C, Peng J, et al. Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis. Circ Arrhythm Electrophysiol. 2008;1(4):258–68. doi: http://dx.doi.org/10.1161/CIRCEP.107.763284. PubMed.

38 Køber L, Thune JJ, Nielsen JC, Haarbo J, Videbæk L, Korup E, et al.; DANISH Investigators. Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure. N Engl J Med. 2016;375(13):1221–30. doi: http://dx.doi.org/10.1056/NEJMoa1608029. PubMed.